Postmarketing surveillance of innovative medicinal therapies in Belgium

Marc VAN DE CASTEELE

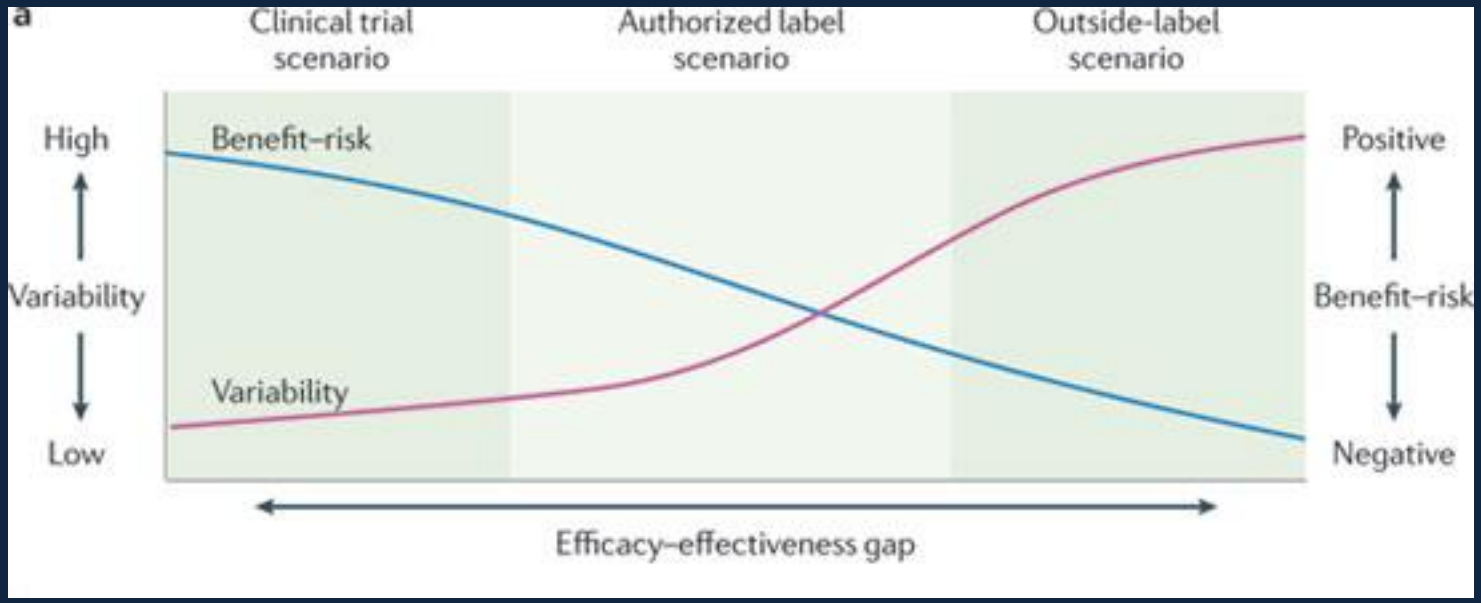
MD PhD

Coordinator HTA pharmaceuticals, RIZIV-INAMI, Brussels

Visiting professor Internal Medicine, Univ. Leuven, Belgium

Introductory (1/2)

The efficacy–effectiveness gap



the external validity of a study !

Nature Rev Drug Disc 2011;10:495-506

Introductory (2/2)

Every post-marketing surveillance
starts with the question
you want to answer !

Follow-up positive reimbursement decisions

In historical order

- Revision of a class of pharmaceuticals
- Individual revision of orphan / added therapeutic value drug
- Reimbursement criteria of orphans
- Combining reimbursement criteria + bills
- Managed Entry Agreements
- Combining reimbursement criteria + clinical data

Revision of a class of pharmaceuticals

Q How adapt reimbursement to new data?

Ex.

- Statins – familial hypercholesterolemia
- Protonpump inhibitors – rebound hyperacidemia
- MRI contrast – pharmacovigilance warning

Who ?
Companies ; pharmacovigilance; signals from real life

Who evaluates?
Our staff + Committee

Individual revision: orphan / added therapeutic value

Q Confirmation on therapeutic value

Ex.

- pegvisomant SOMAVERT in acromegaly
- pirfenidon ESBRIET and nintedanib OFEV
  for idiopathic pulmonary hypertension
- adefovir HEPSERA and entecavir BARACLUDE for hepatitis B
- icatibant FIRAZYR hereditary angio-oedema
- galsulphase NAGLAZYME for mucopolysaccharidosis type VI
- drotrecogine alfa XIGRIS for septic shock

The Lancet 2011 Drug withdrawal sends critical care specialists back to basics.

Who ?

Companies + doctors; Belgian/European real life study

Who evaluates?

Our staff + Committee

Reimbursement criteria of orphans (1/2)

Individual requests + renewals

Via a Orphan College

- half field specialists
- half insurers doctors

Collecting clinical data on paper forms

Future: less paper work

Reimbursement criteria of orphans (2/2)

Q demographic and pharmacological follow-up

Ex

- alglucosidase MYOZYME for Pompe's disease
- tafamidis VYNDAQEL for transthyretine amyloidosis
- carglumic acid CARBAGLU for primary NAG synthase deficiency

Who ?
staff

Who evaluates?
Orphan College + our staff + Committee

Combining reimbursement criteria + bills (1/2)

Individual requests
combined with payments done

Data managers needed.
Privacy needed.

Combining reimbursement criteria + bills (2/2)

Q Are we paying in real life the effects that studies promise?

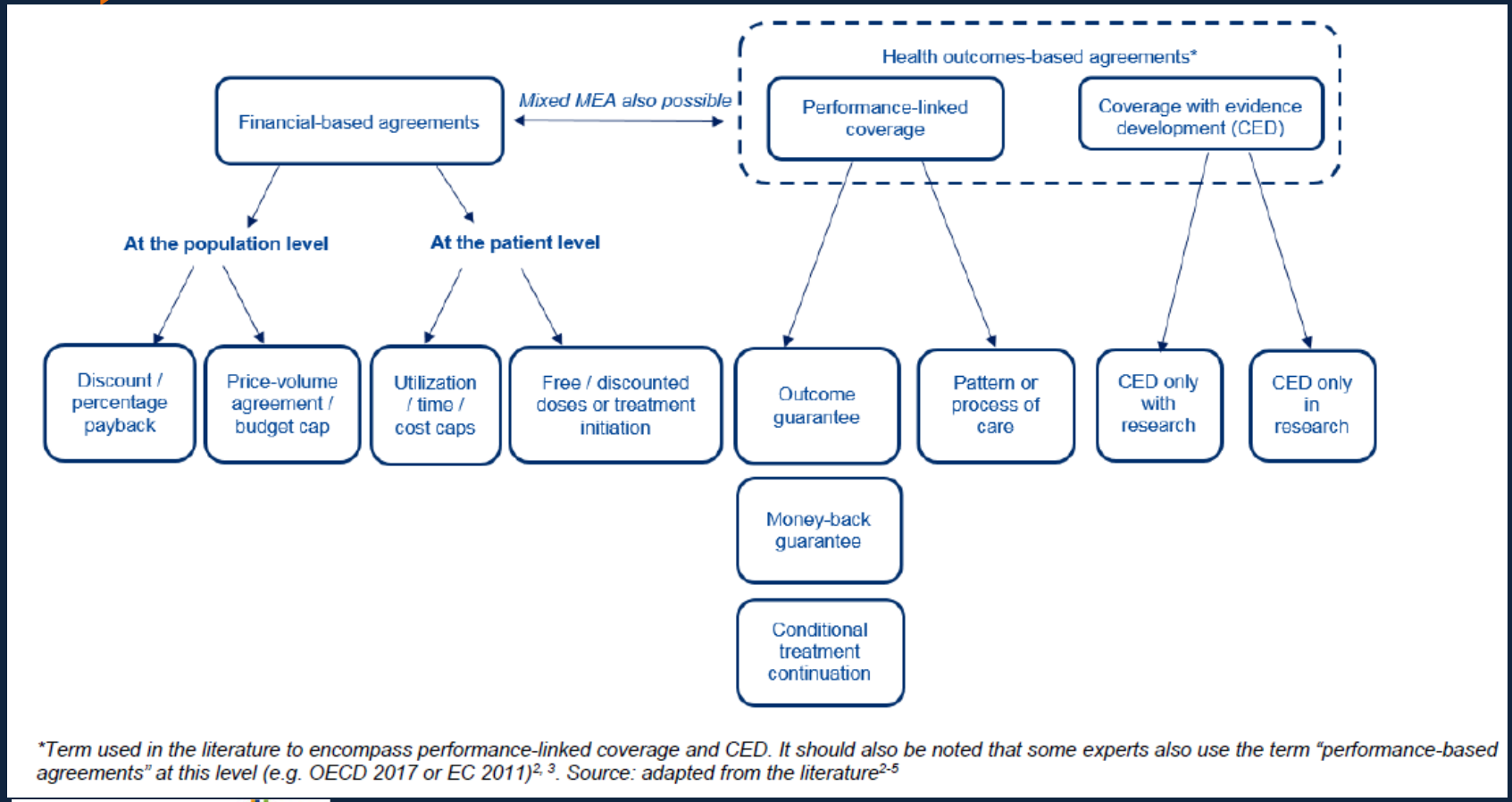
Ex

- **omalizumab XOLAIR for severe asthma**
- **lenalidomide REVLIMID for 5q- myelodysplastic syndrome**

Who ?
Insurers + our staff

Who evaluates?
our staff + Committee

Managed Entry Agreements (1/2)



Term used in the literature to encompass performance-linked coverage and CED. It should also be noted that some experts also use the term "performance-based agreements" at this level (e.g. OECD 2017 or EC 2011)[2, 3]. Source: adapted from the literature[2-5]

2017

Managed Entry Agreements (2/2)

Q Are uncertainties solved ?

Ex

- ruxolitinib JAKAVI myelofibrosis
- axitinib INLYTA renal cell carcinoma
- ponatinib ICLUSIG multiple myeloma
- brentuximab ADCETRIS for various types of lymphoma

Who ?

? Companies + doctors

? Insurers + our staff

Who evaluates?

Contract Group + our staff + Committee

Combining reimbursement criteria + clinical data (1/3)

= work in progress
You ask for additional patient data in hospitals.

Combining reimbursement criteria + clinical data (2/3)

Q What is the efficacy in real life? How is the drug used ?

Ex

- hepatitis C inhibitors
  - criteria (genotype; fibrosis; …)
  - combined with outcome = Sustained viral response
    - after 12 weeks + after 1 year

- anti-TNF and other biologicals in rhumatoid arthritis
  - criteria (flare up; co-medication;….)
  - combined with Disease Activity Score DAS 28

- spinal muscular atrophy: registry with neuro-pediatric scales

Combining reimbursement criteria + clinical data (3/3)

Who ?
doctors + insurers

Who evaluates? (not yet done)
Doctors + our staff + Committee

Results

- **Revision of a class of pharmaceuticals**

pharmacovigilance

- **Individual revision of orphan / added therapeutic value drug**

Scientifically interesting but no constraints for the company; small samples; no major consequences

- **Reimbursement criteria of orphans**

Easy check; keeping it up to date ! ; reimbursement adaptations

- **Combining reimbursement criteria + bills**

Minor consequences

- **Managed Entry Agreements**

More financial than scientific implications till now

- **Combining reimbursement criteria + clinical data**

Long-term vision

Future: turning existing registries (mucoviscidosis; HIV; multiple sclerosis……) into drug registries

Major consequences ?

Some major consequences

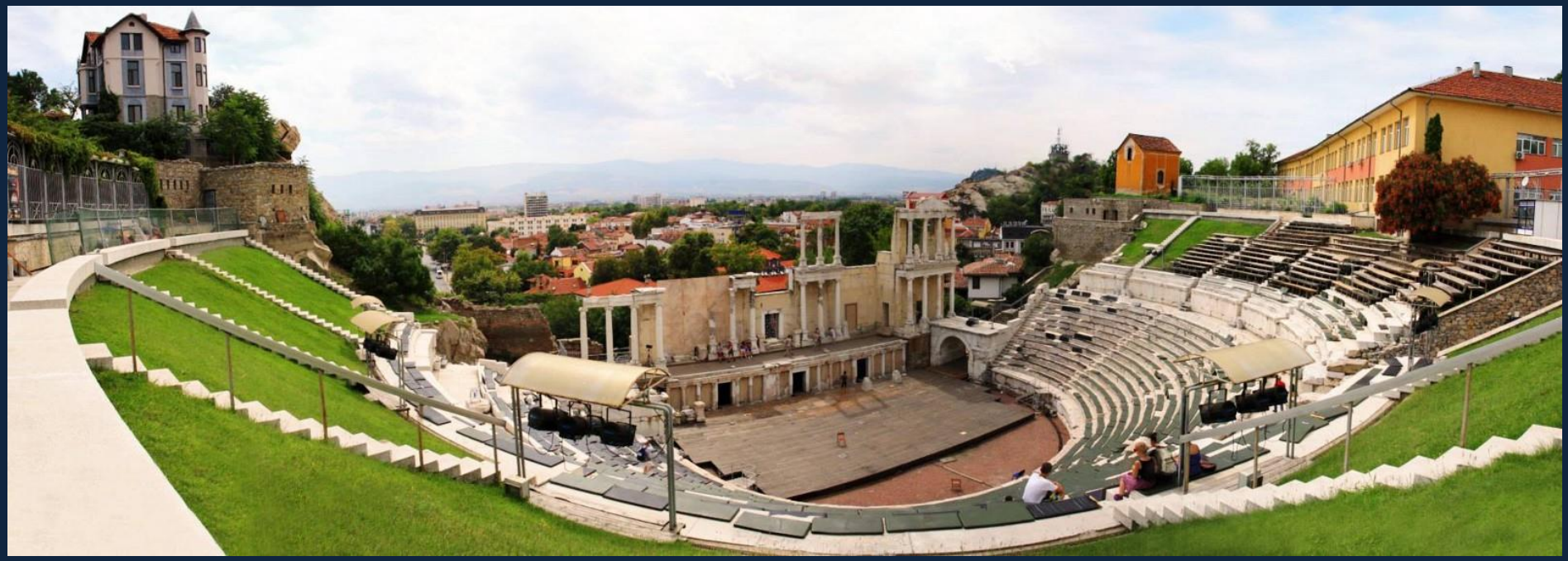
expansion / limitation of reimbursement

e.g. galsulphase NAGLAZYME: cohort closed

e.g. icatibant FIRAZYR more preventive use

carglumic acid CARBAGLU more diagnostic use in more centres

Thank you all for your attention !



Plovdiv

Belgium